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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,450	11/27/2000	Wolfgang Fleischer	228.1007	9935

20583 7590 12/22/2004

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EXAMINER
KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,450	FLEISCHER ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22,32,33,36-41,51,55-61,64-68 and 71-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,32,33,36-41,51,55-61,64-68 and 71-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9-10-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 9-10-04 is acknowledged.

Claims included in the prosecution are 22, 32-33, 36-41, 51, 55-61, 64-68 and 71-74.

Upon consideration, the 112 rejections are withdrawn.

The obviousness type double patenting rejection over the claims of 09/701,220 as set forth in the previous office action is maintained in abeyance to the filing of terminal disclaimer.

Claim Rejections - 35 U.S.C. ' 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 22, 32-33, 36-41, 51, 55-61, 64-68 and 71-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP (0639373) in combination with either

knight (5,049,388) or Radhakrishnan (5,049,389) or Prince (5,290,540); or vice versa (Knight or Radhakrishnan or Prince each in view of EP).

EP teaches the same composition. The composition contains liposome encapsulated povidone iodine (abstract and entire article). What is lacking in EP is the teaching of the application of the composition to treat the infections of lower respiratory tract caused by microbes. However, EP teaches the administration of the composition to mucous membranes (page 2, lines 1-3).

As pointed out before. Knight discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-5 microns. The drugs include antibiotics, antiviral agents and steroids (note the abstract, Tables I and II, examples and claims).

As also pointed out before, Radhakrishnan discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-5 microns. The drugs include antibiotics, antiviral agents and steroids (note the abstract, Examples and claims).

Prince discloses liposome aerosol formulation for the delivery of drugs to respiratory tract. The particle sizes are 1-10 microns. The drug combination includes antibiotics, antiviral agents and steroids (note the abstract, Examples and claims).

In the absence of showing unexpected results, it is deemed obvious to one of ordinary skill in the art to use an anti-septic agent and a wound healing promoting agent (encapsulated in liposomes) taught by EP to any part of the body including the respiratory tract, which has a microbial infection and a wound with the expectation of

reasonable success since the references of Knight, Radhakrishnan and Prince show the common knowledge in the art of using a combination even for the respiratory tract. One of ordinary skill in the art would have been motivated to use PVP-iodine taught by EP as a drug in the liposomal compositions of Knight, Radhakrishnan or Prince with the expectation of obtaining similar results since PVP-Iodine is a known anti-septic agent as shown by EP. EP also does not teach the administration of the composition for the infections which occur during remodeling or repairing the lower respiratory tract. However, it is deemed obvious to one of ordinary skill in the art that the wound healing compositions can be applied during any state wherein the wounds are susceptible to infectious agents, with the expectation of similar anti-septic effect.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant once again argues that skin or eye tissue is not equivalent to the tissue found in the lower respiratory tract. This argument has been addressed before. In essence, although the composition in EP is for external use, EP clearly teaches on page 2, lines 1-9 that the preparations are meant for application to the mucous membranes in humans and furthermore, EP is directed to the treatment of eye conditions. This is suggestive of the safe application of the compositions even for nasal or oral or tracheal mucous tissues. Furthermore, EP at the same location teaches that different antibiotics and antiseptic agents are known for the topical treatment of infectious diseases and that while antibiotics quite often lead to patient sensibilization, antiseptic agents such as PVP-iodine can prevent resistances and that they are much more rarely allergenic, as compared to antibiotics. The safe nature and the effectiveness of the liposomes and the

safe nature of the anti-microbial povidone iodine is obvious from the combined teachings of the references and hence one of ordinary skill in the art would be motivated to use the compositions containing PVP-iodine of EP by inhalation route taught by Knight or Radhakrishnan or Prince. For the same reason, applicant's comparison of liposome encapsulated iodine to shampoos and soaps are not persuasive. Furthermore, the examiner points out that applicant himself have not demonstrated the safety and effectiveness of the composition when administered internally. Instant specification contains only in vitro data, that too against a single organism. It is interesting to note that in instant claim applicant recites 'mercury containing compound' and 'formaldehyde releasing compound'. Aren't these compounds toxic to humans?

Applicant argues that none of the secondary references teaches or suggests liposomes containing povidone iodine, much less that such povidone iodine-containing liposomes can be used in the methods of the invention for treating an infection in the lower respiratory tract. According to applicant they merely teach that liposomes can be administered to the lung and they do not teach or suggest that povidone iodine can be administered to the lung or lower respiratory tract. Furthermore, according to applicant none of the substances taught by Knight, Radhakrishnan or Price to be administered to the lung in liposomes are similar to povidone iodine, which is an aggressive oxidizing antiseptic and none of the types of compounds disclosed by Knight, Radhakrishnan or Price are equivalent to the type of compound that is povidone iodine, no comparison can be made between the suitability to administer any of the compounds taught by Knight. These arguments would have been persuasive if applicant has shown through in

vivo studies, the safe and effectiveness of povidone iodine. However, instant specification does not contain any in vivo studies. As pointed out before, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

3. Claims 22, 32-33, 36-41, 51, 55-61, 64-68 and 71-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP (0639373) in combination with either knight (5,049,388) or Radhakrishnan (5,049,389) or Prince (5,290,540); or vice versa (Knight or Radhakrishnan or Prince each in view of EP) as set forth above, in further combination with WO 85/00112.

The teachings of EP, Knight, Radhakrishnan and Prince have been discussed above.

WO teaches the administration of vaporized microbicidal agent such as povidone-iodine for the treatment of the symptoms of a viral or bacterial infection. The administration is by nasal route (abstract and claims, claims 1 and 7 in particular).

It would have been obvious to one of ordinary skill in the art to administer the liposomal compositions containing povidone-iodine since the reference of WO shows

that povidone-iodine can be administered safely by inhalation route to treat viral and bacterial infections.

Applicant's arguments have been fully considered, but are not found to be persuasive. Arguments regarding Knight, Radhakrishnan and Price have been addressed above. According to applicant, contrary to the Examiner's contention, the International publication teaches that microbicidal agents, including povidone iodine, can be administered by inhalation of a stream or heated air containing the agents to the nasal passages only, which are in the upper respiratory tract. Applicants also note that the heated air component is as an important part of the methods described in the International publication, as are the microbicidal agents. Further according to it is clear that the administration is only to the nasal passages, not to any other part of the respiratory tract, much less the lower respiratory tract. These arguments are not found to be persuasive since and instant claims do not exclude heated air. Even assuming they did, the examiner points out that WO is combined for its teachings of the safe administration povidone iodine internally, that is through nose and not for its teachings of heated air. With regard to applicant's second point, the examiner points out that it would be obvious to anyone that when a compound vapors are inhaled through the nose, those vapors would not just stop at the nose, but would get into the respiratory tract which according to applicant includes even trachea and applicant has not shown that to be otherwise.

The declaration of Dr. Wolfgang Fleischer which states that the compounds disclosed by the cited references are not comparable to povidone iodine and not

suggestive that povidone iodine could be administered safely to the lower respiratory tract are not found to be persuasive since as discussed above, the reference of WO shows that one could inhale povidone iodine safely through the nasal cavity and the reference of EP teaches the effectiveness of povidone iodine against bacteria and viruses.

4. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone

number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK